

**REMARKS**

**I. Status of the Claims**

Claims 16-35 are currently pending and under examination.

Applicants amend claim 16 and several of the dependent claims merely to rephrase portions of those claims for additional clarity, as described further in the sections below. None of the amendments presented herein narrows the scope of any pending claim in this application. Moreover, the amendments are supported by the application as a whole. (See, for instance, the specification at page 6, lines 4-15, and the original claims 1-15.) Indeed, the amended claims are simply alternative methods of phrasing the originally claimed elements, as would be apparent to one of ordinary skill in the art.

Applicants also insert new claim 35, which is supported by the application as a whole, *inter alia*, at page 8, lines 6-18. Applicants respectfully request the entry of the claim amendments and new claim.

**II. Replacement Drawings for Figures 1, 3, 5, 7, and 8**

The Examiner objects to Figures 1, 3, 5, 7, and 8, asserting that they have "poor resolution" and requesting better resolution replacements. (Office Action at page 2.)

Applicants herein provide replacements for all 9 figures, using original scans of the electrophoresis gels in Figures 1, 3, 5, 7, and 8. Hence, Applicants request the withdrawal of this rejection.

**III. The Pending Claims are Definite under 35 U.S.C. § 112, Second Paragraph**

The Office rejected several claims as allegedly indefinite. (Office Action at pages 2-4.) Applicants traverse all of those rejections and discuss each term or phrase the Office objects to in the sub-sections that follow.

Applicants first point out, however, that claims need only define the patentable subject matter with a degree of particularity and distinctness that is reasonable, not exact. (M.P.E.P. § 2173.02, emphasis in original.) Moreover, claim terminology must be analyzed “not in a vacuum” but in light of (a) the application’s disclosure, (b) the prior art, and (c) the understanding of those of ordinary skill in the art. (*Id.*) Therefore, “[a]pplicants are given a great deal of latitude” in their choice of language. (See M.P.E.P. § 2173.05(e).) For example, lack of antecedent support from the earlier claim language or specification taken alone is insufficient to warrant a § 112, second paragraph. (*Id.*)

**Claim 16**

The Office rejects claim 16 due to several different words or phrases. The Office asserts that “the multimers,” “multimer-forming therapeutic proteins,” “the multimer bands,” and “the gel” each lack antecedent basis. Applicants traverse because, according to the M.P.E.P. at § 2173.05(e), lack of antecedent basis and preceding a word by “the” does not necessarily mean that a claim is indefinite. For instance, components that are inherent in other elements of the claim are definite. The M.P.E.P. illustrates that “the surface” in the phrase “the surface of said sphere” is definite because it is understood that spheres have surfaces. (M.P.E.P. § 2173.05(e).) Analogously, “gel electrophoresis,” as recited in claim 16, inherently uses a gel. Thus,

referring to that gel as “the gel” later in the same claim does not render the claim indefinite. Similarly, it is understood from the claim language that “multimer-forming proteins” will form “multimers.” Thus, placing the word “the” in front of “multimers” does not make claim 16 indefinite. Again, in claim 16, gel electrophoresis is used to “fractionate” multimer-forming proteins. Hence, it is understood that the multimers will form various bands on the gel, or “multimer bands.” Hence, placing the word “the” in front of “multimer bands” does not make the claim indefinite. Finally, claim 16 recites that a “Western blot analysis” will be performed. That method inherently uses a “blotting membrane.” Thus, the phrase “the blotting membrane” does not render the claims indefinite. Applicants also note that the metes and bounds of “multimers” in general are set forth at length in the instant disclosure. (See, for instance, page 3, lines 14-24.) Despite these rejections, Applicants have removed the word “the” or altered the grammatical structure of portions of claim 16 where that was possible solely in order to advance prosecution.

The Office also rejected claim 16 due to the word “therapeutic” in front of “proteins” and the word “suitable” in front of “dye.” Because those words are in fact unnecessary for one of ordinary skill in the art to understand the claims, Applicants have simply removed them from claim 16, as well as from dependent claims 17-19, rendering this rejection moot. In any event, the M.P.E.P. states that the modifier “suitable” in front of a claim term does not render the modified term indefinite if one of ordinary skill in the art, reviewing the specification, would be able to ascertain its metes and bounds. (See M.P.E.P. § 2173.03, at page 2100-206, left column, discussing a “suitable liquid.”) Accordingly, here, one of ordinary skill in the art reviewing the instant disclosure would

be able to determine the type of dyes that are appropriate for resolving protein bands in the instant agarose gel electrophoresis from the disclosure. (See the specification at page 4, lines 30-35, and the instant working examples.)

The Office contends that the term "submarine" renders the claims indefinite. However, "submarine" directly modifies the word "electrophoresis." Further, "submarine electrophoresis" is a type of electrophoresis procedure that is known in the art. (See, for example, U.S. Patent No. 5,549,806 to Chen et al., of record, in the title, abstract, and preamble of claim 1.) Thus, one of ordinary skill would understand the meaning of this term on its face. Moreover, one of ordinary skill in the art would understand that the "submarine electrophoresis" is not related to the "blot sandwich" described at page 9 of the application because the "blot sandwich" is part of the Western blot procedure and not part of the electrophoresis procedure.

As to the phrase "chosen from," Applicants also note that it is definite language, though Applicants' amendments to claim 16 delete the phrase, rendering this rejection moot. In fact, analogous claim language is exemplified in the M.P.E.P. (See Example 20, p. AI-66 of the May, 2004, edition.)

The Office objects to the last phrase of the claim reciting that "multimer bands are visualized immunochemically after a Western blot analysis by an immunochemical method chosen from . . ." Applicants submit that one of ordinary skill in the art would understand, in light of the specification, that multimer bands can be visualized by Western blot immunostaining on the blotting membrane or with dyes in the gel. (See the disclosure at page 4, lines 30-35, for example.) Thus, the original claim is definite.

However, to advance prosecution, Applicants have modified the grammatical structure of this portion of claim 16.

The Office also contends that the relationship of the alternative methods of staining (on the blotting membrane or on the gel) is unclear. Applicants submit that one of ordinary skill in the art, reading the instant disclosure, would recognize that they are simply alternatives. Here, Applicants direct the Office to the instant disclosure, including the working examples, which set forth the metes and bounds of this portion of claim 16. For instance, page 4, lines 30-35 introduces the two methods of staining. Pages 8-11 and 13-16 describe each of those methods in more detail. Figures 4 and 6 show densitometric quantitations obtained from each method, while page 17, lines 21-35, discusses how the two staining methods compare in terms of safety and sensitivity.

Finally, the Office asserts that claim 16 omits a step of quantitative determination of the multimers. Applicants assert that this optional step is inherent in the recitation of the preamble that the method is intended for "qualitative and quantitative" determination. But, solely to speed prosecution, Applicants remove the recitation in the preamble and add a quantitation step to the body of the claim. Because the original claim recited that the method was for "qualitative and quantitative determination," moving the optional step to the body of the claim does not narrow its scope.

#### Claims 21 and 23

The Office rejected claims 21 and 23, asserting that "it is not clear whether the recited agarose gels are the same gels used in the parent claims" or are additional gels. (Office Action at page 3.) Applicants point out that those claims are each definite in light of the specification at page 6, lines 30-33, and page 11, lines 26-29, and from claims 21

and 23 themselves, which state that the agarose gel "is employed for separating the [fibrinogen or von Willebrand factor] multimers." Nevertheless, Applicants amend those claims, as well as claim 22, which contains a similar recitation, solely to speed prosecution. The amendments merely re-phrase the claims and do not narrow their scope.

Claims 27 and 28

The Office rejected claims 27 and 28, due to the recitation of the alternatives of staining the gel or blotting the membrane. Applicants refer the Office to the comments above in response to the Office's objections to that portion of claim 16. The blotting and dye staining are alternative procedures, as explained above.

Claim 28

The Office also rejected claim 28 because of the way the word "employed" is used in the sentence. The Office contends that it is not clear which of the gel and the backing sheet is "employed" for the staining of the gel. Applicants submit that the claim is clear on its face to one of ordinary skill in the art as simply reciting the type of gel system that may be stained. Further, the specification sets forth examples of how the staining is performed using a commercially available agarose gel on a backing sheet. (See, for example, page 12, line 35, to page 13, line 20.) Thus, the metes and bounds of claim 28 are clear. Moreover, those of ordinary skill in the art are familiar with agarose gel products and would understand the purpose of the backing sheet. Nevertheless, solely to advance prosecution, Applicants have re-phrased the claim so as not to affect the claim scope.

Claim 29

The Office rejected claim 29, asserting that “the agarose gel employed for immunostaining” and “the blotting process” lack antecedent basis. Applicants submit that those terms are clear on their face as relating to the “Western blot analysis” of the “agarose gel” recited in claim 16. It is inherent that a “Western blot analysis” has a “blotting process” associated with it in which a blot is taken of a gel. Thus, according to the policy of M.P.E.P. § 2173.05(e), there is no need to correct claim 29. Nevertheless, solely to advance prosecution and for additional clarity, Applicants have slightly re-phrased the claim. That amendment does not affect the claim’s scope.

Claims 30-32

Finally, the Office rejects claims 30-32, asserting that it is not clear what “bands” are referred to in the recitation of “the bands.” Applicants assert that it would be clear to one of ordinary skill in the art reading these claims that “the bands” are those discussed in claim 16: the bands that result from the electrophoresis and are visualized either by immunostaining or by a dye. (See the figures of this application for illustration.) Thus, there is no need to amend claims 30-32. They are clear on their face.

Nevertheless, Applicants have amended those claims to recite “the multimer bands” solely to speed prosecution. Accordingly, Applicants respectfully request the Office to withdraw all of these § 112, second paragraph, rejections.

**IV. Claims 16-27 and 30-34 are Unobvious over Connaghan in view of Krizek & Rick**

The Office rejects claims 16-27 and 30-34 over an article by Connaghan et al. (“Connaghan”; *Blood* 65: 589-597 (1985)) in view of an article by Krizek & Rick (*Thrombosis Res.* 97: 457-462 (2000)). Applicants traverse this rejection.

A *prima facie* case of obviousness must satisfy three requirements. See M.P.E.P. § 2143. First, the cited references teach or suggest each and every limitation of the claims. Second, there must be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine their teachings and, third, a reasonable expectation of success in performing the combination. Both the motivation and the expectation of success must also be found in the references themselves or in the knowledge generally available to one of ordinary skill in the art; not in the application being examined. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); M.P.E.P. § 2142. Accordingly, the references must be viewed without the benefit of hindsight afforded by the claimed invention. M.P.E.P. § 2141.

Connaghan and Krizek & Rick do Not Teach All of the Claim Elements

Here, the Office relies on Connaghan for “qualitative and quantitative electrophoretic determination of von Willebrand factor and fibrinogen using a continuous agarose gel stained with a suitable dye.” (Office Action at paragraph bridging pages 4 and 5.) The Office acknowledges that Connaghan does not teach Western blotting. (Office Action at page 5.) The Office relies on Krizek & Rick for teaching detection of von Willebrand factor by Western blot. (*Id.*)

However, the Office overlooks that neither reference teaches a “submarine electrophoresis [procedure] using a continuous, homogeneous agarose gel free of lumps” as Applicants claim. An example submarine electrophoresis procedure of the present application is described, *inter alia*, at page 7, lines 6-26, in which the buffer is re-circulated with a pump and maintained at fairly constant temperature. The cited



articles, in contrast, simply teach standard horizontal gels. In addition, it is evident from the figures of Krizek & Rick, for instance, that its gels contain lumps or uneven polymerization, or that they are deformed during electrophoresis, because several of the lanes of bands are unevenly stained. (See, for instance, lanes 3-5 of Figure 1 and all of the lanes of Figure 2, in which the bands do not run evenly.)

The Office also overlooks that Connaghan's Coomassie blue stained gel strip did not reveal "multimers" of fibrinogen. Instead, only the more sensitive autoradiogram was able to detect multimers. (See the great difference in the first two lanes at the left of Figure 1 marked "a.r." for autoradiography and "c.b." for Coomassie blue, for example.) Connaghan comments that, in contrast to the stained gel, "[t]he autoradiogram of the same gel strip was more sensitive . . . and additional bands were noted that correspond to higher polymers." (Connaghan at page 591, column 1.) . (See Figures 1-4 and 6-8.) Hence, Connaghan strongly teaches away from "visualizing" bands "by a dye in the gel" as Applicants claim. Indeed, one of ordinary skill in the art reading Connaghan would conclude that dyes cannot be used to determine multimers effectively.

Because Connaghan and Krizek & Rick do not teach all of the claim elements, this rejection is not a *prima facie* case of obviousness. The articles fail the other two requirements of obviousness as well.

There is No Motivation to Combine Connaghan with Krizek & Rick

In order to support a motivation to combine references, "it is incumbent upon the Office to identify some suggestion to . . . make the modification." *In re Mayne*, 104 F.3d at 1342, citing *In re Jones*, 958 F.2d 347, 351 (Fed. Cir. 1992). In other words, the

mere fact that the references *can* be combined or modified does not itself render the combination obvious. *In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). Instead, motivation to combine requires a teaching that the combination is *desirable*, not just that it is feasible. *Winner v. Wang*, 53 U.S.P.Q.2d 1580, 1590 (Fed. Cir. 2000). In *Winner*, the Court of Appeals for the Federal Circuit also pointed out that references teaching away from the instant invention may alone defeat a claim of obviousness. *Id.*

There is no teaching in either Connaghan or Krizek & Rick of using a “submarine electrophoresis using a continuous, homogeneous agarose gel free of lumps.” Thus, the two papers cannot provide any objective teaching that would make this element desirable. Moreover, the Krizek & Rick paper seems satisfied with the uneven bands and lumps that appear in its Figures 1 and 2, and accordingly provides no motivation to change the procedure to avoid them.

#### There is No Reasonable Expectation of Success

Finally, if one were, solely for the sake of argument, to combine the teachings of Connaghan and Krizek & Rick, there would be no reasonable expectation of success in “visualizing” multimers “by a dye in the gel” after a “submarine electrophoresis” procedure, for example, because Connaghan shows in its Figure 1 that Coomassie blue staining did not reveal fibrinogen multimers.

In summary, for all of the above reasons, Applicants claims are unobvious and Applicants respectfully request the withdrawal of this rejection.

**V. Claims 28 and 29 are Unobvious over Connaghan, in view of Krizek & Rick, and in view of Riley & Provonchee**

Finally, the Office rejects claims 28 and 29 over Connaghan in view of Krizek & Rick as well as Riley & Provonchee. (Office Action at page 6.) Applicants traverse this rejection for the same reason as the rejection above.

As just discussed, this combination of references does not suggest the present method in which multimers are determined via submarine electrophoresis. (See the section above for a full discussion.) Riley & Provonchee does not bridge the gap in Connaghan and Krizek & Rick's teachings because it relates merely to methods of packaging and protecting gels from damage during shipment and storage. It does not teach specific methods of using gels or performing electrophoresis.

Accordingly, Applicants also request the withdrawal of this rejection.

**CONCLUSION**

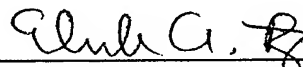
In view of the foregoing amendments and remarks, Applicant respectfully requests reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: July 25, 2005

By:   
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**Attachments:      Petition for a Three-Month Extension of Time and fee payment  
Replacement Drawings (nine sheets for Figures 1-9)**